

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

Please replace the third full paragraph on page 3 with the following amended paragraph:

--FIG. 1 is a graph which illustrates the pharmacodynamic effect (testosterone suppression) obtained by subcutaneous injection in rats of a suspension of ~~Teverelix®~~ Teverelix trifluoroacetate according to the invention; and--

Please replace the fourth full paragraph on page 3 with the following amended paragraph:

--FIG. 2 is a graph which illustrates the sustained release of the peptide ~~Teverelix®~~ Teverelix. for several weeks in rats injected with the suspension of ~~Teverelix®~~ Teverelix trifluoroacetate according to the invention.--

Please replace the first full paragraph on page 6 with the following amended paragraph:

-- A specific discovery was that a highly concentrated aqueous suspension of the peptide of the formula Ac--D--Nal--D--pCIPhe--D--Pal--S- er--Tyr--D--Hci--LeuLys(iPr)--Pro--D--Ala--NH₂ (~~Teverelix®~~ Teverelix, a GnRH antagonist) as a trifluoroacetate (TFA) or sulfate salt does not, as might be expected by its hydrophobic character, form a gel but instead forms a microcrystalline milky suspension which is easy to inject parenterally in animals or humans, and which releases the active principle over several weeks (see FIGS. 1 and 2). Such behavior is not elicited by other salts such as the acetate, which result in the expected, but unwanted, formation of gels with poor bioavailability in vivo.--

Please replace the third full paragraph on page 6 with the following amended paragraph:

--200 μ L of 5% mannitol were added to approximately 15 mg of the LHRH antagonist ~~Teverelix®~~ Teverelix trifluoroacetate. The mixture was stirred using vortex during one minute and a flowing milky pearly suspension was obtained. The suspension is made of microcrystals of about 10 μ m length. Microcrystals may clump together to form urchin like structures. The suspension was injected in rats (1 mg) sub-cutaneously and provided the pharmacodynamic effect of testosterone suppression for more than 45 days (FIG. 1). The pharmacokinetic analysis showed a sustained release of the peptide for several weeks (FIG. 2).--

Please replace the fourth full paragraph on page 6 with the following amended paragraph:

-- 200 μ L of water were added to approximately 15 mg of the LHRH antagonist ~~Teverelix®~~ Teverelix trifluoroacetate. The mixture was stirred using vortex during one minute and a flowing milky pearly suspension was obtained.--

Please replace the first full paragraph on page 7 with the following amended paragraph:

--200 μ L of water were added to approximately 15 mg of the LHRH antagonist ~~Teverelix®~~ Teverelix acetate. The mixture was stirred using vortex during one minute and a transparent gel was obtained. The addition of 20 μ L of TFA (3 mols/mol) to the gel resulted in the formation of a fluid, flowing milky pearly suspension.--

Please replace the second full paragraph on page 7 with the following amended paragraph:

-- 200 μ L of 100 mM TFA were added to approximately 15 mg of the LHRH antagonist ~~Teverelix®~~ Teverelix acetate (2 mols/mol) to obtain a flowing milky suspension. In addition, mixing 200 μ L of 75 mM TFA with approximately 15 mg of the LHRH antagonist ~~teverelix®~~ Teverelix acetate (1.5 mol/mol) resulted in a transparent gel being

obtained after mixing. In another study, 100 μ L of TFA of various concentrations were added to 7.5 mg of the LHRH antagonist ~~teverelix®~~ Teverelix acetate, with the TFA/Teverelix molar ratio ranging from 1 to 3. A flowing milky suspension was obtained with molar ratios of 1.6, whereas gels were obtained at other molar ratios.--

Please replace the third full paragraph on page 7 with the following amended paragraph:

--200 μ L of 150 mM TFA were added to amounts of the LHRH antagonist ~~Teverelix®~~ Teverelix acetate ranging from 5 to 30 mg (concentration ranging from 25 to 150 mg/ml). A flowing milky suspension was obtained with concentrations up to 100 mg/ml.--

Please replace the fourth full paragraph on page 7 with the following amended paragraph:

--200 μ L of 150 mM TFA were added to approximately 15 mg of the LHRH antagonist ~~Teverelix®~~ Teverelix acetate (3 mols/mol) and a flowing milky suspension was obtained after mixing. The suspension was freeze-dried over-night. 200 μ L of water or 5% mannitol were added to the lyophilisate and a flowing milky suspension was obtained after mixing and reconstitution.--

Please replace the first full paragraph on page 8 with the following amended paragraph:

--1 mL of 150 mM TFA were added to approximately 75 mg of the LHRH antagonist ~~Teverelix®~~ Teverelix acetate (3 mols/mol) and a flowing milky suspension was obtained after mixing. The suspension was freeze-dried over-night. 1 mL of water and 0.2M acetate buffer pH 4.0 were added to the lyophilisate and a flowing milky suspension was obtained after mixing and reconstitution. These suspensions were stable for at least 3 days at room temperature.--

Please replace the second full paragraph on page 8 with the following amended paragraph:

-- 100 μ L of a 250 mM H_2SO_4 were added to 7.5 mg of the LHRH antagonist ~~Teverelix®~~ Teverelix acetate (5 mols/mol) and a flowing milky suspension was obtained after several hours. The suspension is made of microcrystals of about 100 μ m length. Microcrystals may assemble together to form urchin like structures. The suspension was freeze-dried over-night. 100 μ L of water or 5% mannitol were added to the lyophilisate and a flowing milky suspension was obtained after mixing and reconstitution.--

Please replace the third full paragraph on page 8 with the following amended paragraph:

-- 100 μ L of a 150 mM trifluoromethane sulfonic acid solution were added to 7.5 mg of ~~Teverelix®~~ Teverelix acetate to obtain a free flowing milky suspension after mixing.--

Please replace the fourth full paragraph on page 8 with the following amended paragraph:

-- 100 μ L of a 150 mM solution of benzenesulfonic acid were added to 7.5 mg ~~Teverelix®~~ Teverelix hydrochloride to give after a mixing a free flowing suspension.--

Please replace the first full paragraph on page 9 with the following amended paragraph:

-- 100 μ L of a 200 mM solution of trifluoroacetic acid solution were added to 2.5 mg of ~~Cetrorelix®~~ Cetrorelix acetate to obtain a milky free flowing suspension.--